Review Article

Genitourinary Syndrome of Menopause Assessment Tools

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Abstract

New therapeutic options are being considered to treat genitourinary syndrome of menopause (GSM), such as vaginal laser, ospemifene, or prasterone, but there is no explicit agreement in the scientific community for its use. Some concerns have arisen on how to evaluate the improvement of GSM symptoms. In 2003, the FDA suggested possible end points for this purpose: change in severity of symptoms, change in vaginal pH, and change in vaginal maturation index (VMI). Contrarily, the most common assessment tools used to quantify severity and improvement of GSM nowadays are the visual analog scale of GSM symptoms, the vaginal health index, and the female sexual function index. In our opinion, subjective and objective variables to evaluate GSM can be differentiated, and not many of the considered objective outcomes are used in the recent literature assessing GSM. There is the possibility that some therapies present only subjective improvement, giving place to a possible placebo effect that is not being evaluated. To conclude, there is a demand to evaluate whether vaginal pH and VMI are enough to assess objectively GSM changes or new objective approaches should be audited.

Keywords: *Assessment tools, genitourinary syndrome of menopause, vaginal laser, vulvovaginal atrophy*

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Introduction

Genitourinary syndrome of menopause (GSM) collects different symptoms and signs related to decreased blood circulating estrogens, comprising from urinary tract symptoms, vaginal dryness, and irritation to dyspareunia and sexual symptoms, provoking to up to 50% of those who suffer it, causing impairment in the quality of life.[1,2]

Mild GSM is usually treated using nonhormonal lubricants and moisturizers, but those present doubtful benefits when facing severe GSM symptoms. The logical treatment to palliate the lack of estrogen is using local estrogen products demonstrated to be the most effective therapy.

Lately, new therapeutic options are being considered to treat GSM symptoms, such as vaginal laser, ospemifene, or prasterone, potential alternatives for those patients where estrogenic therapies are not recommended.[3]

A vast amount of literature is emerging, primarily related to vaginal laser, assessing the safety and efficacy of these new options. However, to date, there is no explicit agreement in the scientific community for its use, since, in 2018, the FDA published an alert highlighting that the efficacy and safety of vaginal laser treatments had not been established.[4]

Furthermore, some concerns have arisen on evaluating the improvement of GSM symptoms when any of the mentioned treatments are used. The assessment tools to measure the success or benefit for each treatment remain a critical hot topic, underlining the lack of consensus among researchers on how we are assessing clinically relevant changes in women presenting with GSM.[5]

Previously, the FDA had summarized possible end points, including change in the severity of symptoms,

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change in vaginal pH, and change in vaginal maturation index (VMI).[6]

This review aims to summarize the present evidence on the diagnostic and assessment tools to evaluate GSM.

Diagnosis of Genitourinary Syndrome of Menopause

The classical diagnostic modality for GSM has been a "clinical diagnosis," including a clinical suspicion when women in menopausal status present symptoms such as burning, dryness, and dyspareunia in the genital tract, and is confirmed through a clinical exploration, observing a pale and dry vulvovaginal mucosa usually with petechiae. It is essential to differentiate from other vaginal conditions that mimic bothersome vaginal conditions such as vaginal lichen sclerosis, vaginal lichen planus, hyperkeratosis, contact dermatitis, vulvar cancer, and vulvar cancer vulvar intraepithelial neoplasm, extramammary Paget disease, and vaginal infections.[7]

Since the clinical diagnosis of GSM started through a report of symptoms from the patients, during the last decades, the GSM diagnosis has been underdiagnosed due to an underreport from patients and unawareness from professionals to seek this problem.[8]

Thereafter, when the diagnosis of GSM is made, a cascade of different treatments starts. The assessment of the GSM improvement was classically made clinically, changing to the next therapeutic step if the women reported no changes.

Today, we are entering a new era where physicians have on board novel therapies such as vaginal laser, prasterone, or ospemifene. Yet, there is no consensus on how to use them. We believe that it is a vital issue to acquire well-designed assessment tools to precisely evaluate the severity of GSM and its improvement when using any treatment, through either subjective or objective tests. The implementation of reliable assessment tools would ultimately bring consistency across scientific evaluation of GSM, allowing to regulate the treatment indications.

Assessment Tools for Genitourinary Syndrome of Menopause

Considering many studies conducted up to date regarding GSM evaluation, the most common assessment tools used to quantify severity and improvement of GSM are the visual analog scale (VAS) of GSM symptoms, the vaginal health index (VHI), and the female sexual function index (FSFI) patient-reported outcomes measure (PROM).

Figure 1: Summary of current and potential assessment tools

Current AT	Potential AT	Subjective	Objective
VAS		0-10	
FSFI		De+Ar+Lu+Or+Sa+Pa	
SF12		Ph+Me	
VHI		Ela+Fv+EI+Mo	pH
Vaginal pH			0-14
VMI			0-100%
	VTb		mm
	VLP		ΔFCVK
	VTu		mm
	VC		kPa

AT: Assessment tools, VAS: Visual Analog Scale on GSM symptoms, FSFI: Female sexual function index (De: Desire, Ar: Arousal, Lu: Lubrication, Or: Orgasm, Sa: Satisfaction, Pa: Pain), SF12: Health-related quality-of-life questionnaire (Ph: Physic [Physical function, physical role, corporal pain, general health], Me: Mental [vitality, social function, emotonial role, mental health]), VHI: Vaginal health index (Fv: Fluid volume, Ela: Elasticity, EI: Epitelial integrity, Mo: Moisture), VMI: Vaginal maturation index, VTb: Vaginal epithelial thickness on biopsy, VLP: Vaginal lamina propia characteristics on biopsy (ΔFCVK: Increased number of fibroblasts, increased amount of collagen, increased degree of vascularization and increase of Ki67), VTu: Vaginal thickness on abdominal ultrasound measure, VC: Vaginal compliance on biopsy (tensile strength), GSM: Genitourinary syndrome of menopause

Depending on the target for each assessment tool, a classification of subjective outcomes and objective outcomes was made:

Assessment tools that considered subjective outcomes, influenced by the patient perception of the complaint, are the most widely used in the scientific evaluation of GSM. Among them, we find the VAS of GSM symptoms evaluation and different PROMS such as the FSFI, assessing six domains of sexuality: desire, arousal, lubrication, orgasm, satisfaction, and pain, and the 12-Item Short Form Survey, which is a health-related quality-of-life questionnaire consisting of 12 questions that measure eight health domains to assess physical and mental health, among others [Figure 1].

It is to note that there is a disagreement on considering VHI, a clinical medical evaluation, as a subjective or objective measure. Some authors consider the VHI an objective measure. Suppose we disaggregate this overall score, in that case, we can observe that in 4 out of 5 variables of the index (vaginal elasticity, fluid volume, epithelial integrity, and moisture), the judgment of the clinical status from the physician is in some manner subjective, remaining just one objective variable which is the vaginal pH measurement.[9]

Instead, not many of the considered objective outcomes are used in the recent literature assessing GSM. The most frequently used is the vaginal pH measurement, recommended since 2003 by the FDA for GSM assessment, and used as a part of the VHI calculation. To assess pH, a piece of litmus paper is placed on the lateral vaginal wall until moistened. A pH of 4.6 or greater indicates vulvovaginal atrophy (VVA), assuming the patient does not have bacterial vaginosis. Premenopausal women without VVA typically have a pH of 4.5 or less.[10]

Another recommended outcome in the 2003 FDA recommendation to GSM evaluation was the VMI, which has not been as successful in the literature as the VHI, considering that it is not usually found in most studies assessing GSM.[11] The VMI assesses the relative proportion of parabasal, intermediate, and superficial vaginal epithelial cell types in a vaginal cytology sample. In premenopausal women, greater than 15% of superficial cells would be considered normal; however, in postmenopausal women with VVA, the typical proportion would be less than 5%. The VMI is usually calculated according to the formula, maturation value: (0 × % of parabasal cells) × (0.5 × % of intermediate cells) × (1.0 × % of superficial cells).[12]

Other objective outcomes had been proposed but scarcely used and only reported in case series studies. Some authors studied vaginal epithelial thickness, composition of the lamina propria, and vaginal compliance: Salvatore *et al*. performed an *ex vivo* histological study on the effects of microablative fractional CO_2 laser on atrophic vaginal samples from five women, concluding that laser can produce a remodeling of vaginal connective tissue without causing damage surrounding tissue.[13]

Contrarily, Mackova *et al*. presented the data from a preclinical trial where pathology analysis was performed to an animal model (ewe), including vaginal thickness, composition of lamina propria, and vaginal compliance, concluding that YAG laser had a comparable increase in vaginal epithelial thickness to sham manipulation in menopausal ewes and none of the interventions induced changes in the vaginal lamina propria.[14]

Finally, few authors attempted to objectively evaluate transvaginal ultrasound to measure the vaginal wall thickness in GSM, suggesting that it could be effective as a histological measurement.[15] Being a promising line of investigation since would bring objectiveness through a noninvasive exploration.

Conclusion

The literature on assessing GSM objectively is scant, and there is a need to develop an objective model for the most appropriate assessment for GSM. From our perspective, there is a demand to evaluate whether vaginal pH and VMI are enough to assess objectively GSM changes or new approaches should be audited.

Although different techniques to evaluate GSM in the actual scientific literature will appear, consistency among studies and clinical trials is needed to facilitate comparisons of results. In our opinion, subjective and objective variables to evaluate GSM can be differentiated. There is the possibility that some therapies present only subjective improvement, giving place to a possible placebo effect. In addition, there is the possibility to find some options where objective outcomes improve with the absence of subjective assessment tools improvement and therefore may be opening the door to complimentary nonphysical therapies.

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Conflicts of interest

There are no conflicts of interest.

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